

Remarks

Favorable reconsideration of this application in view of the amendments to the claims and the remarks below is respectfully requested.

The specification has been amended to incorporate by reference only those documents that are available to the public. In particular, the reference to Serial No. 08/009,264 has been deleted since it is duplicative of the disclosure in EP 621,337, Serial No. 08/322,679 has been identified by issued patent number and Serial No. 60/084,705 has been identified by its corresponding WO application number. Copies of the front pages of EP 621,337 and WO 99/58705 are enclosed for the convenience of the Examiner.

The non-elected claims have been canceled without prejudice.

Claims 36-38, 72, 87, 88, 89 and 97 stand rejected under 35 USC 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is traversed in part as discussed more fully below. The individual rejections are discussed serially.

1. In Claim 36 the "and" before pH has been deleted.
2. Claim 37 has been amended to clarify that it is only a portion of the acid groups of the polymer that have reacted with the base. Accordingly the remaining "unconverted" acid groups are on the polymer.
3. The Examiner has required a quantification of the term "essentially insoluble." This requirement is respectfully traversed. The polymers used in the instant invention are pH dependent polymers. That means that their solubility is dependent on the pH of the medium in which they are residing and the term "essentially insoluble" merely specifies to one skilled in the art which polymer to choose.
4. In Claims 87, 88 and 89 the Examiner states that it is not clear as to what the % is based on, the total weight of the polymer, matrix or what. Applicants

believe the claim is clear that it is the weight percentage of the matrix, however the claim has been amended to clarify this position.

5. Claim 91 has been amended to include the generic form of the tradenames. This rejection is respectfully traversed. The names used in the claim are not tradenames and are the generic names used for the substances. See for example, the entry for Calcofluor white M2R in the 1997 Sigma catalog listed under Fluorescent Brightener 28.
6. The Examiner requested that in Claim 88 the "if" after 75% be changed to "of". It is believed that this should actually occur in Claim 87 and accordingly Claim 87 has been amended.
7. The Examiner has requested that abbreviations be spelled out, including DNA, RNA, and those used in Claims 70 and 72 (1). This requirement is respectfully traversed in part. DNA and RNA are accepted abbreviations used in their ordinary sense and meaning and one of ordinary skill in the art would know what is intended. The abbreviation NPV in Claim 72 is spelled out. Each of the remaining letter combinations is the name of a specific virus and cannot be spelled out.

Claim 70 has been amended so that the term "EPB" no longer appears. The term is "EPV." Basis for this amendment is found in the specification on page 7, line 4.

It is believed that the claims as amended are no longer subject to this rejection. Reconsideration is respectfully requested.

Claims 36-44, 46-48, 52-54, 56, 60, 63-70, 84, 87-89, 92, 93, and 95-98 are rejected under 35 USC 102(e) as being anticipated by Rheume et al for the reasons of record. This rejection is respectfully traversed.

First, Applicants note that Claims 45, 49-51, 55, 56-59, 71-78, 81-83, 85, 86, 90 and 91 remain in this application and are free of this rejection. Therefore once they are free of the rejections under 35 USC 112, second paragraph, discussed above, it is presumed that if they are placed in independent form containing all the limitations of the claims on which they are dependent, they would be in condition for allowance.

The basis of the rejection is that Rheume utilizes the instant components, including the same polymers and the same base. However the process used to make the insecticidal process is different, and a different product is obtained.

The instant invention relates to a process where a slurry of undissolved polymer is mixed with all the remaining ingredients and then spray-dried to obtain the desired product. In this way, a coated matrix is obtained. Even when base is used, the polymer is never fully solubilized (page 9, lines 5-10). In contrast, Rheume teaches that the polymer is completely dissolved and then mixed with active ingredient and precipitated to obtain an encapsulated product. In the instant invention, the base is used to partially solubilize the polymer. In Rheume, the base is used to make the polymer precipitate. Thus neither the process or the product of the instant invention is taught or suggested by Rheume.

Reconsideration is respectfully requested.

Copy of specification, page 7, 15-24, and claims showing changes made.

AcMNPV E2 is described in EP 621337, ~~and co-pending U. S. Serial No. 08/009,264, filed January 25, 1993,~~ which is incorporated herein by reference. AcMNPV V8 and V8vEGTDEL are described in U.S. Patent 5,662,897 which is incorporated herein by reference. V8vEGTDEL-AalT is described in EP 697170-A1 and co-pending U.S. Serial No. 08/322,679, filed July 27, 1994, now US patent 5,965,123. AcMNPV Px1 is described in ~~co-pending provisional U.S. Serial No. 60/084,705, filed May 8, 1998,~~ WO 99/58705 which is incorporated herein by reference.

36. (Twice Amended) A process comprising

(a) preparing an aqueous mixture containing a pesticidal agent, a pH-dependent polymer, a base, optionally a plasticizer, optionally an ultraviolet protector, optionally an activity enhancer, optionally a glidant, and water;

wherein the polymer

(4) contains ester groups and free carboxylic acid groups,

(5) is partially solubilized due to the action of the base, and

(6) has solubilization pH greater than about pH 5.5;

wherein the mixture's pH is less than the polymer's solubilization ~~and~~ pH; and

(b) drying the mixture to produce a pesticidal matrix.

37. (Twice Amended) A process as described in Claim 36, wherein in the mixture, after the base and polymer's acid groups have interacted, less than about 10% of the acid groups of the polymer have been converted to salts.

70. (Twice Amended) A process as described in Claim 69, wherein the double stranded enveloped DNA virus *Entomopoxvirinae* is an entomopox virus (EPV) selected from the group consisting of *Melolontha melolontha* EPV, *Amsacta moorei* ~~EPB~~ EPV, *Locusta migratoria* EPV, *Melanoplus sanguinipes* EPV, *Schistocerca gregaria* EPV, *Aedes aegypti* EPV, *Chironomus luridus* EPV, and mixtures thereof.

87. (Twice Amended) A process as described in Claim 36, wherein the matrix comprised, on a percentage-weight-basis of the matrix, from about 1% to about 50% of the pesticidal agent, from about 5% to about 50% of the polymer, from about 0% to about 25% of the plasticizer, from about 0% to about 30% of the ultraviolet protector, from about 0% to about 75% ~~if~~ of the activity enhancer, and from about 0% to about 15% of the glidant.

90. (~~Twice~~ Thrice Amended) A pesticidal matrix comprising on a percentage-weight-basis of the matrix, from about 1% to about 50% of a pesticidal agent, from about 5% to about 50% of a pH-dependent polymer, from about 0% to about 25% of a plasticizer, from about 0% to about 30% of a ultraviolet protector, from about 0% to about 75% of a activity enhancer, and from about 0% to about 15% of a glidant; wherein the polymer contains ester groups and free carboxylic acid groups, is partially solubilized due to the action of a base, and has a solubilization pH greater than about pH 5.5.

91. (Twice Amended) A pesticidal matrix as described in Claim 88, wherein the matrix comprises, on a percentage-weight-basis of the matrix, from about 5% to about 35% of the pesticidal agent, from about 10% to about 45% of the polymer, from about 0% to about 25% of the plasticizer, from about 0% to about 20% of the ultraviolet protector, from about 0% to about 45% of the activity enhancer, and from about 0% to about 10% of the glidant.

If the Examiner believes a telephone call to the undersigned would favorably advance the prosecution of this application or narrow any outstanding issues, he is respectfully invited to call the undersigned at the telephone number indicated below.

Respectfully submitted



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CERTIFICATION UNDER 37 CFR 1.8(a)

I hereby certify that this paper and the documents referred to as enclosed therein are being deposited with the United States Postal Service on the date written below in an enveloped addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

October 16, 2001  
Date

Ann Giovanelli  
Ann Giovanelli

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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>(51) International Patent Classification <sup>6</sup> :</b><br><b>C12P 21/02, C12N 15/63, 1/21, A61K 31/715</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <b>A1</b> | <b>(11) International Publication Number: WO 99/58705</b><br><b>(43) International Publication Date: 18 November 1999 (18.11.99)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <b>(21) International Application Number:</b> PCT/US99/09914<br><b>(22) International Filing Date:</b> 7 May 1999 (07.05.99)<br><b>(30) Priority Data:</b><br>60/084,705 8 May 1998 (08.05.98) US<br><b>(71) Applicant (for all designated States except US):</b> AMERICAN CYANAMID COMPANY [US/US]; 5 Giralda Farms, Madison, NJ 07940 (US).<br><b>(72) Inventors; and</b><br><b>(75) Inventors/Applicants (for US only):</b> BRENNAN, Lynn, A. [US/US]; 8 Moores Mill-Mt. Rose Road, Pennington, NJ 08534 (US). DIERKS, Peter, M. [US/US]; 262 Daleview Drive, Yardley, PA 19067 (US). MCINTOSH, Arthur [US/US]; 1212 Eldson Drive, Columbia, MO 65203 (US).<br><b>(74) Agents:</b> ROBINSON, Joseph, R. et al.; Darby & Darby P.C., 805 Third Avenue, New York, NY 10022-7513 (US). |           | <b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).<br><br><b>Published</b><br><i>With international search report.</i> |
| <b>(54) Title:</b> RECOMBINANT BACULOVIRUS-BASED INSECTICIDES                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>(57) Abstract</b><br><p>The present invention provides isolated recombinant <i>Plutella xylostella</i> baculovirus for use as insecticidal agents. Preferably, a recombinant baculovirus according to the invention has incorporated within its genome a gene encoding an insecticidal toxin. The invention also provides insecticidal compositions and formulations comprising recombinant <i>Plutella xylostella</i> baculoviruses and methods for killing insect pests and for reducing insect infestation of crops.</p>                                                                                                                                                                                                                                                         |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |

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(54) **Codon optimized DNA sequence for insect toxin AalT.**

(57) This invention provides for the construction of a codon optimized DNA sequence encoding the insect-specific toxin Androctonus australis insect toxin (AalT). The codon optimized sequence is then inserted into an insect virus. A susceptible insect which ingests such a modified insect virus will cease feeding on plants due to a toxin-induced paralysis at an earlier time than an insect which ingests a wild-type insect virus lacking an AalT gene.

**EP 0 621 337 A1**





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|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|---------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|
| <b>E 4886</b><br>[RT]   | <b>ETHYLENEDIAMINE-TETRAACETIC ACID Zinc-Disodium Salt</b><br>Plant Cell Culture Tested<br>[14025-21-9] $C_{10}H_{12}N_2O_8ZnNa_2$ FW 399.6                                                                           | 100 g 12.05<br>500 g 44.10                                                       | <b>F 1019</b><br>[RT]                                         | <b>D-(-)-FRUCTOSE</b><br>(D-Levulose; Fruit sugar)<br><b>Crystalline</b><br>Contains less than 0.05% glucose by enzymatic assay<br>Plant Cell Culture Tested<br>[57-48-7] $C_6H_{12}O_6$ FW 180.2                                                                                                                                                                                                                                                                                    | 100 g 7.05<br>500 g 12.55<br>1 kg 20.95<br>5 kg 78.95    |
| <b>F 0638</b><br>[RT]   | <b>FERRIC SULFATE</b><br>(Iron [III] sulfate)<br>Plant Cell Culture Tested<br>[10028-22-5] $Fe_2(SO_4)_3$ FW 399.9                                                                                                    | 250 g 44.80<br>500 g 74.50<br>1 kg 123.95                                        | <b>F 9642</b><br>[RT]                                         | <b>FUMARIC ACID</b><br><b>Free Acid</b><br><b>Crystalline</b><br>Plant Cell Culture Tested<br>[110-17-8] $C_4H_4O_4$ FW 116.1                                                                                                                                                                                                                                                                                                                                                        | 100 g 9.65<br>500 g 13.15                                |
| <b>F 7388</b><br>[RT]   | <b>FERRIC TARTRATE</b><br>Plant Cell Culture Tested<br>[2944-68-5] $Fe_2(C_4H_4O_6)_3$ FW 555.9                                                                                                                       | 100 g 15.10<br>500 g 59.15<br>1 kg 106.30                                        | <b>G 7520</b><br>[RT]                                         | <b>D-(-)-GLUCOSE</b><br>(Dextrose; Corn sugar)<br><b>Anhydrous;</b><br><b>Mixed anomers</b><br>Plant Cell Culture Tested<br>[492-62-6] $C_6H_{12}O_6$ FW 180.2                                                                                                                                                                                                                                                                                                                       | 1 kg 14.20<br>5 kg 38.10<br>10 kg 54.80<br>25 kg 120.60  |
| <b>F 8263</b><br>[2-FC] | <b>FERROUS SULFATE Heptahydrate: 99+%</b><br><b>Crystalline</b><br>Plant Cell Culture Tested<br>[7782-63-0] $FeSO_4 \cdot 7H_2O$ FW 278.0                                                                             | 50 g 4.90<br>100 g 7.75<br>500 g 24.20<br>1 kg 41.80                             | <b>G 9273</b><br>[RT]                                         | <b>L-GLUTAMINE</b><br>(L-2-Aminoglutaric acid)<br><b>Minimum 99% (TLC)</b><br><b>Crystalline</b><br>Plant Cell Culture Tested<br>[56-85-9] $C_5H_{10}N_2O_3$ FW 146.1                                                                                                                                                                                                                                                                                                                | 25 g 14.10<br>100 g 37.25<br>250 g 78.00<br>500 g 139.25 |
| <b>F 0518</b><br>[2-FC] | <b>FERROUS SULFATE/CHELATE SOLUTION (100X)</b><br>Contains 2.785 g/L $FeSO_4 \cdot 7H_2O$ and 3.725 g/L Ethylenediaminetetraacetic Acid, $2Na \cdot 2H_2O$<br>Sterile-filtered<br>Plant Cell Culture Tested           | UNIT SIZE<br>500 ml 6.45<br>1 L 10.25                                            | <b>G 1150</b><br>[RT]                                         | <b><math>\beta</math>-GLYCEROPHOSPHATE</b><br>(Glycerol 2-phosphate)<br><b>Disodium Salt: Hydrate</b><br>Less than 0.1% L- $\alpha$ -isomer<br>Plant Cell Culture Tested<br>[819-83-0] $C_3H_7O_6PNa_2$ FW 216.0                                                                                                                                                                                                                                                                     | 25 g 20.20<br>100 g 54.20<br>500 g 232.45                |
| <b>F 1397</b><br>[2-FC] | <b>FLUORESCCEIN DIACETATE</b><br><b>Crystalline</b><br>Plant Cell Culture Tested<br>[596-09-8] $C_{24}H_{16}O_7$ FW 416.4                                                                                             | US \$ UNIT PRICE<br>1-5 6-11 12+<br>500 ml 6.45 5.80 5.20<br>1 L 10.25 9.20 8.20 | <b>G 6143</b><br>[RT]                                         | <b>GLYCINE</b><br>(Aminoacetic acid; Aminoethanoic acid; Glycocol) <b>Free Base</b><br><b>Essentially ammonia-free</b><br><b>Crystalline</b><br>Plant Cell Culture Tested<br>[56-40-6] $C_2H_5NO_2$ FW 75.07                                                                                                                                                                                                                                                                         | 100 g 12.60<br>500 g 19.10<br>1 kg 31.40                 |
| <b>F 1522</b><br>[2-FC] | <b>FLUORESCCEIN ISOTHIOCYANATE</b><br><b>Isomer I</b><br>(Fluorescein 5-isothiocyanate)<br>Suitable for use in fluorescent protein labeling.<br>Plant Cell Culture Tested<br>[3326-32-7] $C_{21}H_{11}NO_5S$ FW 389.4 | 100 mg 16.30<br>250 mg 30.35<br>500 mg 51.65<br>1 g 90.85                        | <b>G 1275</b><br>[RT]                                         | <b>GLYCYLGLYCINE</b><br><b>Free Base</b><br><b>Crystalline</b><br>Plant Cell Culture Tested<br>[556-50-3] $C_4H_8N_2O_3$ FW 132.1                                                                                                                                                                                                                                                                                                                                                    | 10 g 12.55<br>100 g 73.15                                |
| <b>F 3397</b><br>[RT]   | <b>FLUORESCCENT BRIGHTENER 28</b><br>(C.I. 40622; Calcofluor white M2R; Tinopal LPW)<br>Plant Cell Culture Tested<br>[4193-55-9] $C_{40}H_{42}N_{12}O_{10}S_2Na_2$ FW 960.9                                           | 1 g 19.90<br>5 g 75.25<br>25 g 293.85                                            | <b>GLYPHOSATE</b><br>See N-(Phosphonomethyl)glycine page 1775 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                          |
| <b>F 8890</b><br>[RT]   | <b>FOLIC ACID</b><br>(Pteroylglutamic acid)<br><b>Approx. 98%</b><br><b>Crystalline</b><br>Plant Cell Culture Tested<br>[59-30-3] $C_{19}H_{19}N_7O_6$ FW 441.4                                                       | 1 g 8.10<br>5 g 10.45<br>25 g 36.40<br>100 g 116.95                              | <b>H 0771</b><br>[2-FC]                                       | <b>HEMICELLULOSE</b><br><b>From Aspergillus niger</b><br>Off-white powder; not completely soluble. Standardized with lactose. Contains cellulase activity.<br><b>Activity:</b> 0.01-0.1 unit per mg solid, using a $\beta$ -galactose dehydrogenase system and locust bean gum as substrate.<br><b>Unit Definition:</b> One unit will liberate 1.0 $\mu$ mole of D-galactose from hemicellulose per hr at pH 5.5 at 37°C (2 hour assay).<br>Plant Cell Culture Tested<br>[9025-56-3] | 1,000 units 9.70<br>5,000 units 23.05                    |

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